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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,926	01/16/2002	Jeffrey R. Sampson	2003309-0027 (Agilent 10	1042

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EXAMINER	
TUNG, JOYCE	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 02/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/052,926	SAMPSON, JEFFREY R.	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35,67-101 and 144-147* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35, 67-101 and 144-147* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The applicant's response filed 12/2/2005 to the office action mailed 8/30/2005 has been entered. Claims 1-35, 67-101 and 144-147 are pending.

1. Claims 1-34, 67-100 and 144-147 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Baldarelli et al. (6,015,714, issued Jan. 18, 2000) in view of Kool (5,714,320, issued Feb. 3, 1998).

Baldarelli et al. disclose a method for sequencing nucleic acid polymer. The description of the method of Baldarelli et al. as listed in claims 1-24 (See Abstract and column 23-24, claims 1-24). Modified base are available including methylated bases (See column 8, lines 44-45). In order to identify the monomers, condition should be appropriate to avoid secondary structure in the polymer to be sequenced (See column 8, lines 53-54).

Baldarelli et al. do not disclose using a circular template, the nucleic acid molecule containing modified nucleotides, which are modified adenosine, modified thymine, modified guanosine and modified cytosine.

Kool et al. disclose a method for synthesis and amplification of DNA and RNA oligonucleotide which involves using circular oligonucleotide template and the nucleotide triphosphates is modified, 2-amino-adenosine-TP (See column 13, lines 50-67). The method uses enzymatic synthesis, which is polymerase enzyme (See column 5, lines 31-46). The teachings of Kool et al. suggest that the synthesized nucleic acid molecules contain modified nucleotides. The products generated from the method include a linear multimer having the desired sequence (See column 14, lines 29-38).

Although the modified nucleotide used in the method of Kool et al. is to make cleavage site (See column 30, lines 57-58), while in the instant invention, the modified nucleotide of the synthesized nucleic acid molecule is to reduce secondary structures in the synthesized nucleic acid, the elements used in the synthesis of nucleic acid are the same.

One of ordinary skill in the art at the time of the instant invention would have been motivated to apply the method of Kool et al. to enzymatically synthesize nucleic acid molecule for the sequencing method of Baldarelli et al. because the method of Kool is directed to efficient, low-cost and large-scale synthesis of linear and circular oligonucleotide (See column 1, lines 21-25). It would have prima facie obvious to provide a nucleic acid molecule with at least one repeat of a nucleotide sequence to be determined, wherein the nucleic acid molecule is enzymatically synthesized using a circular template and the nucleic acid molecule contains modified nucleotides.

The response argues that Baldarelli et al. do not disclose "at least one repeat of a nucleotide sequence to be determined" and it would be desirable to sequence a molecule that contained multiple amplified copies of a single nucleic acid of interest and nothing in Kool teaches or suggests the feature of "at least one repeat of a nucleotide sequence to be determined". Although Baldarelli et al. do not disclose the limitation, which is argued above, Kool, discloses a method for synthesis and amplification of DNA and RNA oligonucleotide, which involves using circular oligonucleotide template. By doing so, one repeat of a nucleotide sequence is produced and multiple amplified copies of a single nucleic acid of interest are produced (See fig. 2).

The response further argues that Baldarelli et al. and Kool do not suggest the feature of "modified nucleotides that reduce secondary structure in the nucleic acid molecule". As discussed in section 1 above, although the modified nucleotide used in the method of Kool et al. is to make cleavage site (See column 30, lines 57-58), while in the instant invention, the modified nucleotide of the synthesized nucleic acid molecule is to reduce secondary structures in the synthesized nucleic acid, the elements used in the synthesis of nucleic acid are the same.

The response argues that the references do not teach the limitations recited in claim 5, "wherein the nucleic acid is an unstructured nucleic acid". Since it is unclear what is meant by the phrase "unstructured nucleic acid", any nucleic acid molecules can be read on this phrase.

The response additional argues that the references do not teach the limitations of claim 34 as recited "wherein the nucleic acid contains 2-aminoadenosine, and 2-thiothymidine". The references do teach modified nucleotide, 2-amino-deoxyadenosine and alphathiotriphosphates (See column 13, lines 55-60).

Thus, one of ordinary skill in the art at the time of the instant invention would have been motivated to apply the method of Kool et al. to enzymatically synthesize nucleic acid molecule for the sequencing method of Baldarelli et al. to make the instant invention. Therefore, the rejection is maintained.

2. Claims 35 and 101 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Baldarelli et al. (6,015,714, issued Jan. 18, 2000) in view of Kool (5,714,320, issued Feb. 3, 1998) as applied to claims 1-34, and 67-100 above, and further in view of Thorp et al. (5,871,918, issued Feb. 16, 1999).

The references of Baldarelli et al. and Kool set forth in section 3 above do not disclose analyzing nucleic acid by electron tunneling.

Thorp et al. disclose a method of detecting a nucleic acid by using electron tunneling (See column 9, lines 30-55). The method may be used in a variety of applications, including DNA sequencing (See the Abstract).

One of ordinary skill in the art would have been motivated to modify the method of Baldarelli et al. by applying electron tunneling as taught by Thorp et al. since the electron tunneling is applied to DNA sequencing. It would have been prima facie obvious to apply the electron tunneling to the method of Baldarelli et al. to make the instant invention for sequencing DNA.

Since there is no specific argument regarding this rejection, the rejection is maintained.

Summary

3. No claims are allowable.

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Joyce Tung J.T
February 11, 2006

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

2/13/06